

**REMARKS**

Reconsideration is requested.

The telephonic interview with the Examiner on January 8, 2008 is acknowledged, with appreciation. Complete copies of the references partially-cited by the Examiner (i.e., Ito (Nature 403, pages 680-684 (February 10, 2000)); Pfister (Investigative Ophthalmology and Visual Science, June 1995; 36(7):1306-16)) are being filed herewith to complete the record.

Claims 1-24 are pending. Claims 6-15 and 22-24 have been withdrawn from consideration. Rejoinder and allowance of any claim defining a method of making and/or using a product defined by an allowable claim, at an appropriate time, are requested. Claims 25-27 have been added. No new matter has been added. Basis for the claims 25 and 26 may be found, for example, on pages 15-16 of the specification. Support for claim 27 may be found throughout the specification, such as pages 3-4, pages 20 and 23 (Example 1), pages 23-25 (Example 2), pages 25-26 (Example 3), pages 26-27 (Example 4), and original claim 4. No new matter has been added.

Claim 1 has been revised to correct the previous definition of the tripeptides. Specifically, the unamended claim 1 allows for a tripeptide with a formula Pro-Pro-Xaa<sub>2</sub> or Xaa<sub>1</sub>-Pro-Pro, which would not be expected as a product of a proline-specific endoprotease, as claimed. Specifically, one of ordinary skill in the art will appreciate that a proline-specific endoprotease produces protein sequences with N-terminal or C-terminal Proline residues, as described for example in Diefenthal et al, World Journal of Microbiology & Biotechnology 11, 209-212 (1995), WO0052147 (such as at page 6, lines 26-31), both of which are of record.

The Examiner will appreciate that endoproteases, such as trypsin, chymotrypsin, pancreatin and prolylendopeptidase, are known in the art and described in the present specification. See third paragraph of page 1 of the specification and the above-noted references of record.

The Examiner is requested to appreciate that the claims define a product by a process of manufacture. Specifically, the claimed product is defined by the manner in which it can be made. The teleconference of January 8, 2008 with the Examiner is believed to have included a brief consideration of the same.

As noted to the Examiner during the teleconference, the applicants believe that one of ordinary skill in the art will appreciate the applicants were in possession of the claimed invention at the time the application was filed. Specifically, one of ordinary skill will appreciate that treatment of a naturally occurring protein-containing composition with a proline-specific endoprotease and a tripeptidase will produce tripeptides of the formulas Pro-Xaa<sub>1</sub>-Xaa<sub>2</sub> and Xaa<sub>2</sub>-Xaa<sub>1</sub>-Pro, as claimed. While the specification does not include a specific and literal description of the these formulas to describe the tripeptides of the invention, the applicants understand that the same should not be required to comply with the written description requirements of Section 112, first paragraph. See In re Hogan and Banks, 194 USPQ 527, 539 (C.C.P.A. 1977) ("This court has held that claimed subject matter need not be described in haec verba in the application to satisfy the written-description-of-the-invention requirement. In re Smith, 481 F.2d 910, 914, 178 USPQ 620, 624 (CCPA 1973)."), In re Wright, 9 USPQ2d 1649, 1651 (Fed. Cir. 1989) ("The specification as originally filed must convey clearly to those skilled in the art the information that the applicant has invented the specific subject

matter later claimed. In re Ruschig, *supra*, 54 CCPA at 1559, 379 F.2d at 996, 154 USPQ at 123. When the original specification accomplishes that, regardless of how it accomplishes it, the essential goal of the description requirement is realized." (citing to In re Smith)).

Withdrawal of the Section 112, first paragraph "written description", rejection of claims 1-5 and 16-21 is requested.

Withdrawal of the Section 112, second paragraph, rejection of claims 6-15 and 22-24 is requested as the Examiner has indicated on page 2 of the Office Action dated August 29, 2007 that these claims have been withdrawn from consideration as allegedly defining a separately patentable invention. Clarification is requested in the event the Section 112, second paragraph, rejection of the withdrawn claims is maintained.

The Section 102 rejections of claims 1-5 and 16-21 over any of Ito (Nature 403, pages 680-684 (February 10, 2000)); Pfister (Investigative Ophthalmology and Visual Science, June 1995; 36(7):1306-16); Haddox (U.S. Patent No. 6,310,041); and St. Pierre (U.S. Patent No. 5,856,308), are traversed. Reconsideration and withdrawal of the rejections are requested in view of the following distinguishing comments.

The cited references fail to teach each and every aspect of the claimed invention, as detailed below.

Initially, the applicants note that the presently claimed invention requires a mixture of tripeptides, as would be understood by one of ordinary skill in the art to be produced from the hydrolysis of a protein-containing composition with a proline-specific endoprotease and a tripeptidase, as claimed.

The Examiner is understood to have asserted in the teleconference of January 8, 2008 that the claims read on peptides, which are larger than tripeptides (i.e., containing more than 3 amino acids), alone which contain a sequence of the formula Pro-Xaa<sub>1</sub>-Xaa<sub>2</sub> or Xaa<sub>1</sub>-Xaa<sub>2</sub>-Pro. The applicants submit, with due respect, that one of ordinary skill in the art will appreciate that the unamended and the amended claims require the presence of a mixture of tripeptides, i.e., sequences of three contiguous amino acids, which includes tripeptides containing an amino- and/or a carboxy-terminal Proline.

The cited art fails to teach the claimed invention. Consideration of the following in this regard is requested.

Specifically, Pfister is understood to describe peptide fragments of alkali-degraded whole cornea which are estimated to be N-acetyl- or N-methyl-blocked Pro-Gly-Pro. See title and page 1310, left column, first paragraph and page 1314, paragraph spanning right and left columns of Pfister. A primary sequence of the tripeptides of Pfister could not be sequenced with N-terminal sequence analysis indicating blockage of the N-terminal amino acid residue. See page 1311, right column, last paragraph. Moreover, the specific activity of chemically synthesized tripeptides PGP, PPG and GPP were an order of magnitude less active in the polarization assay than the N-blocked N-acetyl- or N-methyl-blocked Pro-Gly-Pro sequences. See Table 3 and the accompanying discussion on page 1312, left column "Synthetic Peptides", of Pfister.

The alkali degraded cornea compositions of Pfister, containing N-acetyl- or N-methyl-blocked Pro-Gly-Pro do not anticipate the claimed invention which requires tripeptides having a formula selected from the group consisting of Pro-Xaa<sub>1</sub>-Xaa<sub>2</sub> and

Xaa<sub>2</sub>-Xaa<sub>1</sub>-Pro, wherein Xaa<sub>1</sub> is a naturally occurring amino acid other than Pro and Xaa<sub>2</sub> is a naturally occurring amino acid. Moreover, the individual chemically synthesized PGP, PPG and GPP tripeptides fail to anticipate the claims which require peptides and tripeptides, as described above.

The claims are submitted to be patentable over Pfister.

The cited Haddox patent appears to be from the same group which authored the cited Pfister reference. The patent is understood to provide complementary peptides for the Pro-Gly-Pro sequence found to be an antagonist of PMN leukocyte chemoattractants. . The patent is understood to teach, in relevant part, the specific neutrophil chemoattractants N-acetyl-PGP, N-acetyl-PGX, N-methyl-PGX, N-methyl-PGP "and small peptide chemoattractants containing proline and glycine". See paragraph spanning columns 2-3 of the patent. The patent is believed to teach compositions containing individual peptides and not a product of the claims containing peptides and tripeptides having a formula selected from the group consisting of Pro-Xaa<sub>1</sub>-Xaa<sub>2</sub> and Xaa<sub>2</sub>-Xaa<sub>1</sub>-Pro, wherein Xaa<sub>1</sub> is a naturally occurring amino acid other than Pro and Xaa<sub>2</sub> is a naturally occurring amino acid.

Withdrawal of the Section 102 rejection of the claims over Haddox is requested.

The claims are believed to be patentable over Ito et al which is not believed to teach tripeptides, as claimed. The reference is believed to teach larger peptides with a "universal cassette motif, for which tripeptide XXX was extensively analysed." See page 681, paragraph spanning left and right columns. One of the cassettes is believed to include Proline. The reference is not believed however to teach tripeptides of the claims or products containing tripeptides and peptides of the claims.

Withdrawal of the Section 102 rejection of the claims over Ito et al is requested.

The claims are submitted to be patentable over St. Pierre which is, like Ito et al, understood to teach peptides of more than three amino acids containing motifs of Pro-Pro-Gly and Pro-Hyp-Gly. See column 2, lines 30-39 of St. Pierre. The patent is also understood to describe copolypeptide triple helix of formula A which contains motifs of  $X_{aa}-X_{bb}-Gly$ , wherein  $X_{aa}$  and/or  $X_{bb}$  could be Proline. See, Formula A and column 4 of St. Pierre.

St. Pierre is not believed to teach or suggest a product of the claims containing peptides and tripeptides having a formula selected from the group consisting of  $Xaa_1-Xaa_2$  and  $Xaa_2-Xaa_1-Pro$ , wherein  $Xaa_1$  is a naturally occurring amino acid other than Pro and  $Xaa_2$  is a naturally occurring amino acid.

Withdrawal of the Section 102 rejection of the claims over St. Pierre is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By:                     /B. J. Sadoff/  
                    B. J. Sadoff  
                    Reg. No. 36,663

BJS:  
901 North Glebe Road, 11th Floor  
Arlington, VA 22203-1808  
Telephone: (703) 816-4000  
Facsimile: (703) 816-4100